Prenatal care

Effectiveness and Implementation

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Effect of prenatal care upon medical conditions in pregnancy

Phillip G. Stubblefield

Introduction

The practice of prenatal health care (regular visits to a health professional throughout pregnancy) is well accepted as essential to the well-being of mother and fetus. This chapter examines in some detail this issue of prenatal care and its effect on maternal medical conditions. First, maternal juvenile diabetes mellitus is presented as an example of the superb benefits that prenatal care can bring to both mother and fetus. This paradigm is then considered with regard to a number of other conditions, including hypertensive disease, assessment of fetal growth, cardiovascular disease, maternal smoking, autoimmune diseases, hematologic disorders, disorders of coagulation, renal disease, neurologic disease, and liver disease. The chapter concludes by acknowledging the need to rigorously evaluate the effectiveness of new therapies and their outcomes in prenatal care.

Historical perspective on prenatal care

Organized prenatal care began in the United Kingdom early in the present century and the structure of visits defined by the British Ministry of Health in 1929 is still practiced (Banta et al., 1984). Prenatal care is comparatively recent in the United States. The first edition of the American classic, Williams' *Obstetrics*, published in 1903, had no section on prenatal care, and only a few pages on the diagnosis of pregnancy (Williams, 1903). By the 13th Edition, published in 1966, prenatal care still received only 12 pages, with the acknowledgment that "before the rise of present-day obstetrics, the physician usually had but one interview with the patient before he saw her in labor and often at that interview merely sought to compute the expected date of confinement" (Eastman et al., 1966). In contrast, a representative current obstetric text includes detailed sections on prenatal care totaling more than 200 pages and several hundred additional pages dealing with specific conditions affecting pregnancy (Gabbe et al., 1996).

Historically, the first focus of prenatal care was to improve maternal safety. The accepted plan of visits, consisting of monthly visits in early pregnancy, becoming more frequent in the mid trimester, then weekly in the last month, was an attempt to detect the most common serious illness of women in pregnancy – pre-eclampsia. Epidemiologic studies support the benefit of this approach, as they appear to demonstrate lower maternal and perinatal mortality for women who receive prenatal care (Greenberg, 1983).

However, the utility of prenatal care in reducing hazards to the pregnant woman has been little examined until relatively recently, and there are comparatively few randomized trials or other studies that demonstrate the global efficacy of prenatal care upon maternal health (Enkin, 1992; Villar et al., 1993). In fact, the authors of a recent systematic review concluded that because healthier women are more likely to receive care, selection bias could explain the apparent benefit (Fink et al., 1992).

The issue of prenatal care's utility was explored in a recent Norwegian study, which evaluated the effectiveness of care in terms of the detection rates for five conditions thought to represent the bulk of non-symptomatic disease in pregnancy and the main reasons for screening pregnant women (Backe and Nakling, 1993). The conditions were: twin pregnancy, placenta previa, breech presentation, small-for-gestational-age (SGA) infant (birth weight $<$ 10th percentile), and pre-eclampsia. The study examined a sample of 1908 women giving birth in one Norwegian county in a 12–month period during 1988–1989. Sensitivity, specificity, predictive values, and prevalence are shown in Table 1.1. The low rate at which pre-eclampsia was detected is directly relevant to this discussion of maternal impact. It is not clear from the article whether the failure to diagnose this condition before hospitalization for labor reflected true failure or was because these women did not develop the signs of pre-eclampsia until labor began (Backe and Nakling, 1993). SGA is another case in point. The very poor ability of prenatal care in this study to detect this problem is disappointing in light of the fact that SGA may also reflect maternal health. However, screening was only carried out by measuring the height of the uterine fundus, not by the frequent use of ultrasound, as is current in the U.S. The effectiveness of screening upon outcome was not reported.

The utility of prenatal care in reducing morbidity from maternal illness in pregnancy depends upon the prevalence of the illness among childbearing women, our ability to detect the illness, and our application of effective therapy or preventive strategies. The economic evaluation of prenatal care is more complicated, and is discussed elsewhere (Bahaug, 1992). Theoretically, prenatal care as currently practiced in the U.S. should be of marked benefit to the pregnant woman. As listed in Table 1.2, screening women for a variety of illnesses is routine

Table 1.1 Effectiveness of prenatal screening for five conditions

Condition	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Prevalence per 100
Twins	94.1	100.0	100.0	99.9	0.9
Placenta previa	57.1	100.0	100.0	99.8	0.4
Breech	69.4	100.0	100.0	99.2	2.5
SGA	13.6	99.5	75.0	91.1	10.1
Pre-eclampsia	74.6	99.5	84.7	99.1	3.5

Source: Backe and Nakling, 1993.

Table 1.2 Summary of pre-pregnancy and prenatal health intervention strategies

Before pregnancy

- ✓ Obtain general medical history, reproductive history.
- ✓ Conduct physical examination.
- ✓ Review outcome of previous pregnancies and assess pregnancy risk. Obtain previous records if any abnormal outcome.
- ✓ Detect previous pregnancy wastage that might have a remediable cause (uterine septum, uterine duplication, incompetent cervix).
- ✓ Perform genetic history, screening for inherited illness and malformations.
- ✓ Provide indicated genetic carrier testing, e.g., cystic fibrosis, Tay-Sachs Disease, hemoglobinopathies.
- ✓ Screen for STDs, including HIV, and counsel about prevention strategies.
- ✓ Determine rubella status. Consider immunization, if patient is using reliable contraception.
- ✓ Screen for hepatitis B; consider immunization.
- ✓ Perform cervical cytology; evaluate and treat abnormal findings.
- ✓ Encourage smoking cessation.
- ✓ Prescribe folate to prevent neural tube defects.
- ✓ Ensure control of blood sugar for women with diabetes mellitus.
- ✓ Counsel about avoiding environmental exposure to volatile household chemical (e.g., paints, oven cleaners, cleaning fluid, lead, other heavy metals).
- ✓ Counsel about avoiding eating raw meat and contact with cat litter (toxoplasmosis).
- ✓ Counsel about common teratogenic drugs (e.g., isotretinoin, valproate).
- ✓ Encourage weight gain for very slender women.
- ✓ Counsel about avoiding exposure to sick children who might have transmissible viral illness.
- ✓ Determine if woman is being abused and arrange help if needed.
- ✓ Screen for use of alcohol and other drugs and arrange treatment if needed.
- ✓ Determine adequacy of living conditions and seek improvement if needed.
- ✓ Advise about automobile safety and encourage wearing of seatbelts.

Early pregnancy interventions

- ✓ Repeat the actions and interventions listed above.
- ✓ Confirm diagnosis of pregnancy and rule out ectopic pregnancy.
- ✓ Perform general and pregnancy-specific physical exam; note uterine size, perform clinical pelvimetry.
- ✓ Determine blood type and screen for blood type antibody (Rh, Kell, other blood group sensitization).
- ✓ Determine hemoglobin or hematocrit, diagnose and treat anemia.
- ✓ Screen for hepatitis A, B.
- ✓ Screen for hemoglobinopathy.
- ✓ Screen for bacteriuria and treat urinary infections.
- ✓ Screen for syphilis, gonorrhea, chlamydia; treat as needed.

- ✓ Screen for tuberculosis; evaluate positives and treat as needed.
- ✓ Screen for HIV, and if positive, offer counseling and treatment, including zidovudine therapy to prevent fetal transmission.
- ✓ Obtain cervical cytology.
- ✓ Screen for bacterial vaginosis and treat with systemic antibiotic.
- ✓ Assess maternal weight and adequacy of nutrition, counsel about diet, obtain additional food sources if needed.
- ✓ Prescribe nutritional supplements: iron, multivitamins containing folate.
- ✓ Perform early pregnancy ultrasound to determine duration of pregnancy.
- ✓ Instruct patient about self care during pregnancy, and signs and symptoms of abnormalities.
- ✓ Assess adequacy of social supports and offer assistance when needed.
- ✓ If previous cesarean section, obtain operative report and determine type of uterine incision, and counsel about vaginal birth after cesarean, if appropriate.

Follow-up visits throughout pregnancy

- ✓ Repeat risk assessment.
- ✓ Provide 12–14 prenatal visits with monitoring of maternal weight, blood pressure, measurement of uterine fundal height, auscultation of fetal heart rate.
- ✓ Determine if adequate maternal weight gain is occurring and counsel to improve nutritional status, if appropriate.
- ✓ Test urine for protein and glucose at each visit.
- ✓ Test for triple marker (alpha fetoprotein, BHCG, estriol) at 15–17 weeks to screen for Down's syndrome and neural tube defects.
- ✓ Perform mid-trimester genetic amniocentesis for women over age 35 and others at increased risk.
- ✓ Perform ultrasound exam at 18–20 weeks to screen for other anomalies.
- ✓ Perform glucose load test (50 gm glucose, one hour blood sugar) at 24–28 weeks to screen for gestational diabetes.
- ✓ Administer Rh immune globulin at 28 weeks to Rh negative, unsensitized women.
- ✓ Rescreen for gonorrhea, chlamydia, syphilis, and group B streptococcus in mid-third trimester.
- ✓ Instruct about the course of normal pregnancy, warning signs, e.g., decreased fetal movement, rupture of membranes, bleeding, uterine contractions.
- ✓ Instruct about, or ensure patient receives instruction in, events of labor and delivery, psychoprophylactic preparation for labor pain, education regarding alternatives for pain relief in labor, education in methods of delivery, and indications for intervention.

Detection and management of specific problems (examples; not inclusive)

- ✓ Rh negative and sensitized: manage with serial antibody titres and amniocentesis, intrauterine transfusion, intentional timed preterm delivery as indicated.
- ✓ Diabetes screen positive: evaluate with GTT, follow with weekly blood sugars, treat with insulin as indicated.
- ✓ Hypertension: assess renal, hepatic function, coagulation, advise rest at home, follow

Table 1.2. (*cont.*)

	closely, hospitalize when needed for intensive monitoring of mother and fetus, and perform intentional preterm delivery if indicated.
✓	IUGR suspected: evaluate with ultrasound, look for causes, treat if possible, monitor, hospitalize and perform delivery early if indicated.
✓	Post-term pregnancy: conduct weekly ultrasound for amniotic fluid volume, perform twice weekly fetal heart rate monitoring (non-stress testing), consider planned induction of labor.

Sources: Enkin et al., 1996; Johnson et al., 1996; PHS, 1989.

in U.S. prenatal care practice. Some of these conditions, such as heart disease or diabetes mellitus, are made worse by pregnancy. Others are not made worse by pregnancy, but the perceived need for prenatal care brings the patient into the health care system and allows early diagnosis and effective intervention. An example is cancer of the uterine cervix. Cervical cytology, done routinely at first prenatal visits, effectively screens for invasive and preinvasive lesions. These lesions, if untreated, may progress to invasive cancer, but effective therapies exist.

The paradigm: maternal juvenile diabetes mellitus

Diabetes provides an excellent example of the benefits of care for both mother and fetus, before pregnancy, during pregnancy, and after delivery. In contrast to most other maternal illnesses that affect or are affected by pregnancy, the history of pregnancy outcomes of diabetes before modern management has been well documented. Before insulin was discovered, patients of reproductive age usually died within 1–2 years of onset of the illness and pregnancy was very rare. As described by Gabbe (1992), J. Whitridge Williams' 1909 summary of the world literature included only 66 pregnancies in 43 women. Half of the mothers died, either during the pregnancy or within the next 2 years, and the overall pregnancy loss rate was 41%. Then in 1921, insulin was discovered, and by 1922 was being used in diabetic children. Successful pregnancy in three cases of women with diabetes was reported by Dr. Priscilla White of the Joslin Clinic in 1932.

Despite the immediate improvements in maternal survival that occurred when insulin became available, perinatal outcome remained poor. In Kramer's (1936) report of 665 cases, stillbirth occurred in 25% and only 43% of the infants survived. Maternal mortality was 4%. Pregnancy in diabetic women was complicated by a high rate of fetal malformations, sudden fetal death in late pregnancy, pre-eclampsia and eclampsia, death from prematurity, and fetal injury and death from macrosomia.

Over the years since, management of the pregnant diabetic has improved dramatically so that perinatal mortality, with the exception of that from fetal malformations, is close to that of the general population (Landon and Gabbe, 1992). With the reduction in perinatal mortality from intrauterine death and prematurity, neonatal deaths from malformation account for 30–50% of perinatal mortality due to maternal diabetes.

Current management of pregnancy in the diabetic woman is described below. There appears to be no randomized trial of the entire plan of management, nor could withholding of care be ethically acceptable, given the very poor outcome of these pregnancies in the past.

Pre-pregnancy care

Major anomalies are increased about four-fold in women with insulin-dependent diabetes, ranging from 8 to 10% compared with about 2.4% in the general population. Central nervous system anomalies, including anencephaly and myelomeningocele, are increased ten-fold, and major cardiac lesions are increased five-fold. Sacral agenesis is increased 200- to 400-fold (Landon, 1996). These anomalies occur during the first seven weeks of gestation, and have been linked to metabolic abnormalities resulting from poor control of the diabetes. Intensive treatment of the diabetes with insulin before pregnancy reduces the rate of these major malformations from the expected 8% or so to the same rate as non-diabetic women.

Assessing the mother's condition before pregnancy is potentially of great benefit to her as well as to the fetus, because pre-existing vascular disease may contraindicate pregnancy. For example, women with diabetes of long duration may have ischemic heart disease. Myocardial infarction in pregnancy may have a mortality rate as high as 50%. Unfortunately, only about 20% of diabetic women with ischemic heart disease present before pregnancy.

Care during pregnancy

Careful regulation of maternal glucose is essential to a good outcome for mother and fetus. Patients follow a strict diet and are taught to monitor their own glucose control with glucose oxidase impregnated test strips and a glucose reflectance meter, measuring their own glucose with a drop of blood obtained by a finger stick before breakfast, lunch, and dinner, and at bedtime. A mix of regular and intermediate action insulin is given, and two to three injections per day are needed to provide normoglycemia without hypoglycemia. Frequent visits and frequent telephone contact with the providers is needed to adjust the insulin dosage. Ultrasound is performed early in pregnancy to confirm gestational age, again at

18–20 weeks to identify anomalies, and at 4–6 week intervals to confirm normal fetal growth.

Prenatal fetal surveillance is carried out beginning at 32–34 weeks to detect fetuses at risk of sudden intrauterine fetal death. Patients whose glucose has not been well controlled or who have vasculopathy or hypertension are thought to be at increased risk for this calamity, and testing begins earlier for them, at 28 weeks. The non-stress test (NST) appears to be the preferred method for prenatal surveillance in the U.S. The fetal heart rate is detected by Doppler ultrasound and printed on a strip chart. Accelerations of at least 15 beats per minute lasting at least 15 seconds indicate a normal or reactive test. If accelerations are absent, the test is considered non-reactive and abnormal. Further testing with ultrasound biophysical profile or a contraction stress test is then indicated.

Formerly, elective preterm delivery was performed to prevent intrauterine fetal death. The timing was based on the severity and duration of the mother's diabetes. Currently, delivery is usually planned for 38–39 weeks after demonstration of the presence of adequate levels of surfactant in amniotic fluid, and sooner if prenatal surveillance indicates fetal jeopardy. Because fetal macrosomia is common and associated with neonatal injury, elective cesarean delivery is favored if ultrasound estimates of fetal weight exceed 4000 grams.

Renal disease is common in women with insulin dependent diabetes and in 5–10% of pregnant diabetics. Screening with creatinine clearance and testing for proteinuria is therefore routine. The majority of diabetic women with renal disease will develop superimposed pre-eclampsia by late pregnancy, requiring expert management, often with prolonged hospitalization and intentional preterm delivery.

Women with diabetic proliferative retinopathy are at increased risk for progression of this eye disease during pregnancy. An ophthalmologic exam is essential in early pregnancy, and laser therapy is performed as needed. Women with severe retinopathy unresponsive to laser therapy are advised to terminate the pregnancy to avoid permanent severe vision loss (Landon, 1996).

Gestational diabetes

Diabetes develops in 2–3% of pregnancies, but the majority of these new cases will be limited to the duration of the pregnancy, hence the term "gestational" diabetes. In the U.S., universal screening of all pregnant women for diabetes is the norm. This is done with a single blood glucose measurement performed one hour after a 50 gm oral glucose load.

The significance of gestational diabetes and whether it is beneficial to screen for it has been disputed in England (Enkin et al., 1996). Women who have no

pre-existing diabetes are probably at little risk during pregnancy. The hazard of gestational diabetes for the fetus is increased risk of macrosomia and related birth injury and neonatal jaundice and hypoglycemia. Risk of macrosomia appears to be reduced by active management of gestational diabetes and insulin therapy if blood glucose levels rise above predetermined levels, but there has been no demonstration that this program reduces neonatal mortality. Further, if gestational diabetes therapy is associated with more cesarean sections for fetal macrosomia, it may increase maternal risk. Regardless of questions about its benefit, however, routine glucose screening has become a part of U.S. practice.

Because as many as 50% of women with gestational diabetes will become overtly diabetic in their later years, screening in pregnancy does provide early identification of a group of women who will benefit from close follow up after pregnancy. Weight loss and exercise may reduce the proportion who will develop overt diabetes and improve their longevity.

Application of the paradigm to other conditions

A variety of other conditions also present opportunities to reduce maternal risk through prenatal interventions. These are discussed below.

Hypertensive disease

Hypertensive disease complicates 5–10% of pregnancies and is therefore the most common medical complication of pregnancy (Sibai, 1996). A variety of hypertensive disorders in pregnancy are recognized. All present a potentially serious risk to the mother and the fetus. These illnesses include chronic hypertension present before pregnancy, pre-eclampsia and eclampsia, and chronic hypertension with superimposed pre-eclampsia. Pregnancy-induced hypertension (PIH) is another term often employed. PIH includes pre-eclampsia or elevated blood pressure alone, presenting for the first time during pregnancy. In addition to the direct effects on the mother, hypertensive illnesses increase the risk of premature separation of the placenta (abruption), which may produce fetal asphyxia and death and places the mother at risk of life-threatening hemorrhage.

Pre-eclampsia

Pre-eclampsia is a systemic vascular disease unique to human pregnancy. It is characterized by hypertension, proteinuria, and edema. It may progress to eclampsia, with convulsions, coma, and death. It also may present as an acute liver disease with associated thrombocytopenia and coagulopathy. This so-called HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) is an especially

severe form of pre-eclampsia that can lead to death over 1–2 days if not treated by intentional preterm delivery and expert supportive care.

Reduced maternal perfusion of the uterus, resulting from vasospasm in the uterine arteries, is common with pre-eclampsia and places the fetus at risk for intrauterine growth restriction (IUGR) and sudden fetal death. Pre-eclampsia is more common in first pregnancies, in women with multiple gestations, and women with diabetes. There is familial predisposition. The cause of pre-eclampsia is unknown, but the currently favored theory of etiology is that it results when placental trophoblast cells fail to invade the muscular walls of the uterine arteries and convert them from high-pressure resistance vessels to low-pressure capacitance vessels. This invasion and conversion occurs as part of a normal pregnancy.

Prevention of PIH and pre-eclampsia

Studies of the utility of prenatal care in reducing pregnancy-induced hypertension exist for adolescent women. Adolescents, especially those under age 16, are at increased risk for pregnancy-induced hypertension. A meta-analysis of comprehensive prenatal care versus "traditional care programs," reported in 1994, identified five such trials published between 1972 and 1987. The summary relative risk for PIH with comprehensive prenatal care was 0.59 (95% confidence interval 0.49–0.72), supporting the conclusion that expanded prenatal services do reduce the occurrence of this illness in adolescent women (Scholl et al., 1994). There is considerable current interest in the possibility of preventing pre-eclampsia with medication. For example, calcium supplementation has been tried. Since the disorder has as part of its pathophysiology an excess of synthesis of thromboxane over prostacyclin, partial inhibition of the prostaglandin synthetase system with low-dose aspirin has also been attempted (Dekker, 1995). Unfortunately, as noted in Chapter 4, large randomized studies have found neither calcium supplementation nor low dose aspirin to be of value in preventing pre-eclampsia.

Screening for hypertension in pregnancy

Routine prenatal care includes determination of maternal blood pressure and urinary protein at each visit for all women. Signs and symptoms of pre-eclampsia are looked for at each visit. Women who develop hypertension are followed more closely, and if blood pressure continues to rise and if proteinuria or edema develop, they will be actively managed as described below.

Management of chronic hypertension

In addition to blood pressure and tests for urine protein at each visit, women with a history of pre-existing hypertension receive additional measures: measurement

of creatinine clearance to assess initial renal function, and possibly, treatment with antihypertensive agents. The most important risk to the woman with chronic hypertension is the development of superimposed pre-eclampsia. If pre-eclampsia does not supervene, vascular disease does not progress, and there is normal expansion of the intravascular volume, then perinatal outcome is little different from that for normal women. The presence of proteinuria indicates that pre-eclampsia is developing. With superimposed pre-eclampsia, the vascular spasm and reduced vascular volume that are the hallmarks of that illness develop, and the outcome of pregnancy is poor. As summarized by Goldenberg (1992), 10–20% of women with mild chronic hypertension (diastolic BP < 110 mm Hg) developed pre-eclampsia, and in that group, 10% had abruption, 33% had an SGA neonate, and 24% had perinatal mortality. The more severe chronic hypertensives (diastolic BP > 110 mm Hg) had a somewhat greater risk for developing pre-eclampsia (28%). Of these, 78% had an SGA baby, all gave birth prematurely at a mean gestational age of 29 weeks, and perinatal mortality was 48%.

Management of pre-eclampsia

Patients diagnosed as having mild pre-eclampsia are prescribed bed rest at home, and monitored at frequent intervals, usually twice weekly with blood pressure and urine protein measurement. If the condition becomes more severe, the patient is admitted to the hospital for bed rest and assessment of vital signs several times per day, laboratory assessment to look for liver or renal involvement, and fetal monitoring with the non-stress test where the fetal heart rate is observed for accelerations. Ultrasound is used to measure fetal dimensions as evidence of appropriate growth, and biophysical parameters are observed. Often, the patient's condition moderates with bed rest in the hospital, and the pregnancy can be allowed to progress for days or even weeks. If either the maternal or fetal condition worsens, labor is induced. Worsening maternal condition might include the development of the HELLP syndrome or progression to eclampsia, which can involve convulsions and coma. This emergency requires seizure prevention with medication, usually intravenous magnesium sulfate in the U.S., and prompt delivery of the infant. Delay in delivery may result in maternal death.

Pre-eclampsia most commonly occurs late in the third trimester, when the fetus is relatively mature and able to survive if intentionally delivered early. However, the condition is also seen early in the third trimester when a favorable fetal outcome is much less certain. Delivery is necessary to cure the illness, but the fetus may die or suffer long-term morbidity from preterm delivery. If delivery is delayed too long, the fetus may die in utero, and the mother may die as well. In this setting, the mother may be managed in an intensive care setting on the labor and delivery

unit, with a battery of laboratory tests every few hours, hourly blood pressure measurement, and continuous electronic fetal heart rate monitoring. Glucocorticoids are given to the mother as this has been shown to increase fetal lung production of surfactant, which reduces the risk of respiratory distress syndrome. Any further deterioration in fetal or maternal condition is taken as an indication for induction of labor or immediate delivery by cesarean section.

Poor fetal growth

Poor fetal growth can indicate a fetal abnormality, but it can also indicate underlying maternal illness with resultant poor perfusion of the fetus. Assessment of fetal growth is a part of routine prenatal care. The height of the uterine fundus is measured with calipers or tape measure at each visit and recorded. Progressive growth is expected. If growth is greater or less than expected, an ultrasound examination is obtained. The fetus is imaged with ultrasound and critical dimensions are measured: the biparietal diameter of the fetal head, circumference of abdomen, and length of femur. By comparison to growth charts, these dimensions can be used to predict the gestational age and determine whether fetal size is appropriate. If fetal size is less than expected, a determination is made as to whether there could be an error in dating the pregnancy based on last menstrual period, or whether the problems truly represent a problem in growth. As will be clearly shown in Chapters 6, 7, and 8, it is important to diagnose growth restriction, as it can lead to intrauterine fetal death or long-term morbidity among survivors.

If growth restriction is confirmed, possible causes are sought. Possible maternal illnesses associated with IUGR include hypertensive disease, maternal cardiac disease, pulmonary diseases, renal disease, hemoglobinopathy, connective tissue disease, inflammatory bowel disease, and other severe gastrointestinal disease with maternal starvation, severe diabetes mellitus, and maternal substance abuse (the most common being cigarette smoking) (Carlson, 1988). If maternal illness exists, it should be treated. Generally, when growth restriction is confirmed, women are hospitalized for bed rest, fetal status is monitored with non-stress testing daily or twice weekly, and ultrasound is repeated at two-week intervals to monitor growth.

Cardiovascular disease

Pregnancy produces dramatic changes in the maternal circulatory system. By mid-pregnancy, plasma volume expands by 40%, red cell volume by 30%, and cardiac output rises by as much as 50%, as compared to the nonpregnant state (Hess and Hess, 1992; Landon and Samuels, 1996). Labor poses additional stress, with cardiac output increasing still further. These normal physiologic changes pose a real hazard for the woman with pre-existing cardiac disease.

The prevalence of heart disease in pregnant women ranges from 0.4% to 4.1%

worldwide, with rheumatic heart disease accounting for about 90% and congenital heart disease the rest (Burlew, 1990). In developed countries, rheumatic fever has become much less common, and many fewer women are entering the reproductive years with this disease. Therefore, an increased proportion of cardiac cases are of congenital origin. With the availability of effective surgical therapy for both rheumatic valvular disease and congenital anomalies of the heart, an increased number of women entering pregnancy have had previous surgical repair of their cardiac lesion. This group generally has reduced risk, but may face special problems, as for example, the need for continuous anticoagulation through pregnancy. Examples of some cardiovascular lesions and their effects in pregnancy are given below.

Diagnosis of heart disease before pregnancy and appropriate management can be expected to reduce the risk to mother and baby. However, we have only historical evidence for this. Mortality in the early part of this century for pregnant cardiac patients exceeded 20%, but fell with introduction of specialty clinics after 1920 (Reid et al., 1972). In his paper, Fitzgerald (Fitzgerald et al., 1951) reported a mortality of 0.85% among cardiac patients followed in a special clinic, but 9% among non-clinic patients. Functional class as defined by the New York Heart Association criteria can be used to predict outcome. Women who are class I and II generally do well during the pregnancy, with appropriate care. Women who are class III and IV are at considerable risk, and in one historical series, 30% died within 10 years.

Acquired valvular heart disease

The most common form of acquired valvular heart disease seen in pregnant women is mitral stenosis as a sequel to rheumatic heart fever. About 25% of cases are first diagnosed during pregnancy when women become symptomatic, with tachycardia, fatigue, dyspnea, tachypnea, and orthopnea, as pressure rises in the left atrium and pulmonary veins. With the progression of pregnancy, patients may decompensate suddenly, developing atrial fibrillation or rapid atrial tachycardia and pulmonary edema. Aortic stenosis is much less common, but is associated with a high mortality rate. If the valve area is recognized before pregnancy as being smaller than a critical size, corrective surgery is recommended. Mitral and aortic insufficiencies are usually well tolerated in pregnancy. Mitral valve prolapse without other abnormalities does not increase risk for mother or fetus.

Congenital heart disease

Atrial septal defect is the most common congenital disease in reproductive age women, and if not associated with other lesions, does not adversely effect outcome. However, women who have developed pulmonary hypertension face in-

creased risk (Hess and Hess, 1992).

Patients with Tetralogy of Fallot have pulmonic stenosis, ventricular septal defect, and aortic override. They are cyanotic because of the right to left shunt, and this typically increases during pregnancy. Prognosis is worse if the hematocrit is over 60%, the oxygen saturation is less than 80%, or if the patient already has had syncopal attacks before pregnancy. Patients with the more severe lesions of this type are at risk for sudden death, especially during labor.

Eisenmenger syndrome, characterized by ventricular septal defect associated with progressive pulmonary hypertension and shunt reversal, poses a very great risk. Women with this syndrome have a 30–50% mortality in pregnancy, typically occurring postpartum, and the infant mortality rate is as high as 40%. These women are advised to terminate the pregnancy. If this is refused, or the condition is not recognized until mid-pregnancy, patients are usually hospitalized for the duration of pregnancy, given supplemental oxygen, anticoagulated, and treated for congestive heart failure if it develops.

Marfan's Syndrome is an inherited autosomal dominant disease, affecting connective tissue. The average age at death is 30, secondary to dissection of the aorta and rupture. Measurement by ultrasound of the diameter of the aortic root is of some help in predicting risk. A woman with a root diameter of less than 40 mm has a better prognosis. Termination of pregnancy is generally advised. If refused, patients are managed with β-blocking drugs, careful monitoring of blood pressure and ultrasound measurement of aortic route diameter, limitation of exercise, and generally, hospitalization from mid-pregnancy onward.

Ischemic heart disease

Myocardial infarction (MI) resulting from ischemic heart disease is very rare in women of reproductive age, but if it occurs during pregnancy, there is a risk of death of 40–50%. Women with previous MI are advised to avoid pregnancy. A woman with a history of MI who wishes to undertake a pregnancy should be fully assessed before pregnancy with studies of myocardial contractility and coronary flow, including cardiac catheterization if it has not already been performed. Consideration could be given to angioplasty before pregnancy for patients with significant coronary occlusion. However, there is little information as to how well women do in pregnancy after these procedures. Women with acute MI during pregnancy have occasionally been reported to survive after emergency coronary artery bypass surgery.

Management of women with heart disease

Preconceptional counseling is advised, with full history and physical exam, basic laboratory tests, including an electrocardiogram, and review of previous records of

assessment and treatment (Hess and Hess, 1992). Ideally, the patient is evaluated by a team that includes a maternal fetal medicine specialist, cardiologist, cardiac surgeon, anesthesiologist, and genetics counselor. Functional class should be established and stress testing and cardiac ultrasound performed to define the lesion. Specific risks to the patient and the potential child should be discussed with the patient and her family. If the patient is on anticoagulant medication, plans should be made to convert to heparin as soon as pregnancy is confirmed. Patients with rheumatic disease are given prophylactic penicillin to reduce risk of recurrence. When pregnancy occurs, other sources of cardiac stress are reduced as much a possible. Management includes increased rest, restriction of sodium, and the use of diuretics and digitalis preparations. If symptoms worsen, the patient may need to be hospitalized for the duration of the pregnancy for more intensive management. Because poor fetal growth is common, growth is followed by serial ultrasound studies. Fetal surveillance with non-stress testing and ultrasound biophysical profiles is provided in the third trimester.

Maternal smoking

As discussed in Chapter 2 and a number of other chapters, smoking is clearly detrimental to the health of the mother over the long term. Although the most important immediate effect of maternal smoking during pregnancy is an increase in the proportion of infants born at low birth weight, it is also associated with pregnancy complications that can endanger the mother, including placenta previa, placental abruption, and premature rupture of the fetal membranes (Cnattingius, 1992). Smoking is readily detected during prenatal care. In this author's experience, middle-class women typically stop smoking when they become pregnant. Demonstration of effective strategies for smoking cessation in higher-risk, low-income groups is problematic (Kendrick and Merritt, 1996).

Autoimmune diseases

These disorders, mediated by an immunologic response to antigens on normal cells, affect 5–7% of the overall population, and several are more common in women than men.

Myasthenia gravis

This is a rare disorder of neurotransmission across the myoneural junction caused by autoantibodies against the acetylcholine receptors in skeletal muscle. The disease typically undergoes remissions and exacerbations, and commonly exacerbates in pregnancy or postpartum (Floyd and Roberts, 1992). It is treated with with corticosteroids and with quarternary ammonium compounds, which inhibit acetylcholinesterase activity. Acute or chronic respiratory failure with the disease

can be life threatening. Anesthesia and surgery present special problems, and expert management is needed during labor and delivery.

Systemic lupus erythematosus (SLE)

SLE is a multi-organ disease characterized by autoantibodies and vasculitis. Maternal autoantibodies produced as a result of SLE may affect the pregnancy. Patients in remission at the beginning of pregnancy and who have not manifested multi-organ disease may do fairly well in pregnancy. However, women with pre-existing lupus nephritis are at serious risk for exacerbation and permanent loss of renal function. Antiphospholipid syndrome also may be seen with lupus, and results in repeated pregnancy losses and markedly increased risk for pre-eclampsia. Although it is difficult to differentiate lupus nephritis from pre-eclampsia, one distinguishing difference is that in lupus nephritis, the levels of serum complement (the system of more than 20 plasma proteins involved in immunomodulation and inflammation) fall, while in pre-eclampsia they remain constant. Women with lupus require expert management and frequent visits through pregnancy, often including prolonged hospitalization in late pregnancy. Slow fetal growth and intrauterine fetal death are a concern, so fetal assessment with ultrasound and non-stress testing should be offered from mid-pregnancy until delivery. High-dose steroids are used to treat exacerbation of the SLE, but because of the overlap with pre-eclampsia, intentional preterm delivery may be needed if the maternal condition worsens.

Antiphospholipid syndrome

This illness is characterized by maternal production of autoantibodies, lupus anticoagulant, and anticardiolipin, and is associated with repeated pregnancy losses from thrombosis in the placental bed, with resulting infarctions of the placenta. It occurs more commonly in women with underlying autoimmune disease, such as SLE, but is also found in women whose only symptom is repeated reproductive failure. It can be successfully treated with low-dose aspirin, and either corticosteroids or low-dose heparin. Both steroids and heparin present special problems in management, and require close follow up and expert management. Even on therapy, these women are at increased risk for superimposed pre-eclampsia and poor fetal growth (Petri, 1997).

Hematologic disorders

Iron deficiency anemia is common in pregnancy because of the increased need for iron from the marked increase in maternal blood volume in later pregnancy and the needs of the fetus. The more severe forms of anemia can lead to high-output

congestive heart failure (Perry and Morrison, 1992). Iron supplementation during the prenatal period is routine in this country.

Megaloblastic anemia, resulting from folate deficiency, is also common in pregnancy, and is associated with reduced maternal blood volume, and abruptio placenta. Folate deficiency has recently been implicated in the causation of the common serious fetal neural tube defects called myelomengocele and anencephaly (Rosenberg, 1992). Supplementation with folate is now routine during pregnancy. Food supplementation with folate is to begin in the U.S. as a strategy to prevent neural tube defects.

Hemoglobinopathies

The sickle cell hemoglobinopathies (HbS S, HbS C, and HbS-Thal) are hemolytic anemias characterized by recurrent painful crises, systemic infection, and infarction of various organ systems. HbS S is the most common, and affects approximately one in 708 African Americans. Generally, these diseases are diagnosed in childhood, but sometimes women become symptomatic for the first time during pregnancy. Management during pregnancy requires close follow up and early aggressive treatment of exacerbations. Crises are managed with blood transfusion if symptoms are severe and unresponsive to conservative management with oxygen, hydration, and analgesia. Prophylactic exchange transfusions to prevent crises are also used. Morbidity from pneumonia, pyelonephritis, cholecystitis, pulmonary emboli, retinal hemorrhages, and superimposed pre-eclampsia are considerable (Perry and Morrison, 1992). There is increased risk for fetal death, so care routinely includes ultrasound assessment of fetal growth and prenatal fetal heart rate monitoring.

Standard prenatal screening includes hemoglobin electrophoresis for all African American women in order to detect all forms of hemoglobinopathy. If carrier status is identified, then paternal testing is also needed to allow for appropriate genetic counseling.

Disorders of coagulation

Bleeding

Von Willebrand disease is an inherited disorder of coagulation caused by abnormality of von Willebrand's factor, a carrier for factor VIII in the coagulation cascade. Both autosomal dominant and recessive inheritance patterns are seen. Three major types are recognized, and severity varies with the type. Factor VIII increases in pregnancy, so postpartum hemorrhage from the uterus is not commonly a problem. However, episiotomy may result in hemorrhage, and cesarean section presents a major risk for bleeding from the surgical incision.

Treatment is with desmopressin, which increases complexing of von Willebrand factor with factor VIII, or with recombinant factor VIII. Cryoprecipitate is used less often because of risk for infection.

Thrombosis

Pregnancy and the postpartum period are times of increased risk for venous thrombosis and thromboembolism. Four inherited conditions are now recognized that increase risk of clotting during pregnancy. Antithrombin III, protein S, and protein C are regulatory proteins that inhibit coagulation. Women with deficiencies of these factors are unable to balance the increase in activation of the coagulation system that normally occurs with pregnancy and are at great risk for thrombosis (Trauscht-Van Horn et al., 1992). A recently discovered point mutation in clotting factor V, factor V Leidin, results in a form of factor V that resists destruction by activated protein C. It is found in 3–5% of the population of European ancestry and constitutes the most common form of inherited predisposition to clotting. Women with this condition are also at very great risk for thrombosis during pregnancy. Patients with any of these conditions commonly are given low dose heparin during pregnancy, and if they have previously experienced thrombosis, will receive full anticoagulation throughout pregnancy (Hirsch et al., 1996).

Renal disease

Chronic renal disease often presents as chronic hypertension. This condition was discussed earlier. Pyelonephritis occurs in 1–2% of pregnancies and can rapidly become life threatening (Samuels, 1996). Approximately 10% of young women have asymptomatic bacteriuria, and of these, up to 40% will develop symptomatic urinary infection in pregnancy. Screening urine cultures is routine in prenatal care. Women who test positive are treated with antibiotics to reduce risk for pyelonephritis. A meta-analysis of 11 trials of antibiotic treatment of asymptomatic bacteriuria in pregnancy reported an 80% decrease in odds for developing pyelonephritis (Enkin, 1992).

Neurologic disease

Cerebrovascular disease, though uncommon in young women, is markedly increased with pregnancy. Prompt evaluation of neurologic symptoms and early diagnosis allow more timely intervention and less mortality (Albert and Morrison, 1992).

Pseudotumor cerebri is exacerbated by pregnancy and may lead to blindness from pressure atrophy of the optic nerves. Diagnosis and treatment with carbonic anhydrase inhibitors or steroids can reduce morbidity.

Seizure disorders affect 0.3–0.6% of pregnancies and 35–40% of these women will have an increased frequency of seizures during pregnancy. Congenital anomalies are increased in women with epilepsy, whether or not they are treated with anti-seizure medication. Some of the anti-seizure medications are teratogenic and most depress folate metabolism. Ideally, women with seizures would have pre-pregnancy evaluation, be changed to medications with the least adverse fetal effects, and have close monitoring with dose adjustment in pregnancy to prevent exacerbation of the seizure disorder.

Pregnant spinal cord injury patients are at increased risk for anemia, decubitus ulcers, urinary infections, venous thrombosis, and autonomic hyperreflexia, and require expert management.

Liver disease

Acute fatty liver of pregnancy is rare but until recently was usually fatal. Of unknown cause, the disease begins with nausea, vomiting, and abdominal pain in late pregnancy, progresses to jaundice, then somnolence and coma (Samuels and Landon, 1996). Disseminated intravascular coagulopathy, acidosis, and severe hypoglycemia are important elements of this disease. Management requires correction of coagulopathy with blood products, and treatment of the hypoglycemia with glucose solutions. Delivery is essential, and labor will be induced, or if the cervix is unfavorable, cesarean section is performed after correction of the coagulopathy.

Conclusion

Although this chapter has addressed some of the major illnesses that may complicate pregnancy, increase risk for mother or fetus, or afford opportunities to improve outcome with early diagnosis and management, it is far from exhaustive. Those wishing to know more are referred to current texts of maternal fetal medicine (Gabbe et al., 1996; Sciarra et al., 1997).

The gold standard for evaluating medical interventions has come to be the randomized clinical trial. Meta-analysis of existing randomized trials of components of prenatal care has been very productive in differentiating therapies that are useless, or even harmful, from those that have been proven to be helpful (Enkin et al., 1996). Ideally, any prenatal care for non-life-threatening conditions should be evaluated in this fashion before being adopted into practice. For example, screening for gestational diabetes and its management should be evaluated with a randomized trial. Most of the conditions discussed in this chapter are life-threatening and effective therapy already exists and is in use for them. Therefore,

randomized trials to demonstrate the value of prenatal care for these conditions are not ethical. However, the effectiveness of these therapies and their outcomes should still be studied in order to detect opportunities for improved care.

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